

Attorney Docket No. 3806-0510-00
Application No.: 09/909,797

REMARKS

With entry of this Amendment, claims 18 and 19 have been canceled, and claims 71-81 have been added. Claims 1, 2, 5-16, 20-46, and 56-81 are pending in this application.

Claims 71 and 72 correspond to cancelled claims 18 and 19, rewritten to follow claim 61, from which they depend.

Claim 73 finds support, for example, at page 4, lines 14-17.

Claims 74-76 find support, for example, at page 11, lines 16-19 and page 12, lines 5-8.

Claim 77 finds support, for example, at page 4, lines 8-14, and in original claim 17.

Claim 78 finds support, for example, at page 4, lines 8-14, and in original claim 26.

Claim 79 finds support, for example, at page 4, lines 8-14, and in original claim 17.

Claim 80 finds support, for example, at page 4, lines 8-14, and in original claim 17.

Claim 81 finds support, for example, at page 4, lines 8-14, and in original claim 10.

The amendments to the claims do not add new matter.

Applicants acknowledge, with appreciation, the indication that claims 10-16, 18-37 (now claims 20-37, 71, and 72), and 59-70 are allowed.

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Claims 1, 2, 5-9, 57, and 58 Are Not Anticipated by Mardiguian

The Examiner rejects claims 1, 2, 5-9, 57, and 58 under 35 U.S.C. § 102(e) as allegedly anticipated by Mardiguian U.S. Patent No. 6,384,021 ("Mardigulan"). Specifically, the Office maintains that Mardiguian discloses compositions of heparin having a molecular weight lying between 2000-4000 daltons, an anti-Xa activity between 100 and 150 IU/mg, and an anti-IIa activity of less than or equal to 10 IU/mg. (Office Action at 3 and 4, *citing* Mardiguian at col. 5, lines 20-23 and col. 6, lines 27-30.) The Office also asserts that the ratio of anti-Xa to anti-IIa activity of the Mardiguian compositions is in the range of greater than 10:1. (Office Action at 3 and 4.)

Applicants respectfully traverse this rejection. "A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently in a single prior art reference." *Verdegaal Bros v. Union Oil Co. of Calif.*, 814 F.2d 628, 631 (Fed. Cir. 1987); *see also* M.P.E.P. § 2131. Because Mardiguian does not disclose all of the elements of claims 1 or 2 (and claims 5-9, 57, and 58 which depend therefrom), Mardiguian cannot anticipate those claims.

Claim 1 recites a composition described, *inter alia*, as having a mean molecular weight of 1500 to 3000 Daltons, an anti-Xa activity in the range of 110 to 150 IU/mg, an anti-IIa activity of up to 10 IU/mg, and an anti-Xa:anti-IIa ratio of greater than 10. Similarly, claim 2 recites a composition described, *inter alia*, as having a mean molecular weight of 1500 to 3000 Daltons, and an anti-Xa activity in the range of 110 to 150 IU/mg.

Mardiguian generally describes a genus of compositions of heparin, having an average MW somewhere between 2,000 and 4,000 Daltons, and an anti Xa activity

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somewhere between 100 and 150 I.U./mg. These ranges overlap with, but are different than, the compositions recited by the pending claims. The Office appears to consider that this mere overlap is enough to render the claims anticipated by Mardiguan. Applicants disagree.

"When the prior art discloses a range which touches, overlaps, or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. To anticipate the claims, the claimed subject matter must be disclosed in the reference with sufficient specificity to constitute an anticipation under the statute." M.P.E.P. 2131.03. Whether the requisite sufficient specificity is present or not is a fact-dependent determination. M.P.E.P. 2131.03.

Mardiguan fails to disclose a single composition that falls within the recited ranges of Applicants' claims. This deficiency of Mardiguan is compounded by the Examples which describe species having *either* an anti-Xa activity of 110 or greater *or* an average molecular weight of 3000 Daltons or less. Mardiguan does not disclose a single species having an anti-Xa activity of 110 or greater *and* an average molecular weight of 3000 Daltons or less.

Moreover, Mardiguan clearly suggests that to achieve an anti-Xa activity of 110 or more, the composition would have to have an average molecular weight of more than 3600. For example, the compositions of Examples 1 and 3 in the Mardiguan table have an anti-Xa of 120 and a molecular weight of 3650; and an anti-Xa activity of 110 and an average molecular weight of 3616, respectively. In comparison, the compositions of Examples 4 and 5 have an average molecular weights of 2,777 and 2,161, respectively,

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with an anti-Xa activity of 100. Thus, based on the teachings of Mardiguan, if one of skill in the art desired a composition with an anti-Xa activity of greater than 110, he would design the composition to have an average molecular weight of more than 3600.

In support of its contention that Mardiguan discloses all elements of Applicants' claims, the Office relies, in part, on claims 1 and 4 of Mardiguan. Applicants submit that this reliance is improper. See *In re Benno*, 768 F.2d 1340, 1346, 226 USPQ 683, 686 (Fed. Cir. 1985) ("The scope of a patent's claims determines what infringes the patent; it is no measure of what it discloses."). Applicants submit that, as described herein, Mardiguan does not disclose Applicants' claimed invention.

In conclusion, Mardiguan discloses compositions having **either** an anti-Xa activity of 110 or greater **or** an average molecular weight of 3000 Daltons or less, but never both. By excluding Applicants' claimed subject matter from the disclosed compositions in this way, the Mardiguan reference necessarily fails to disclose every limitation of the rejected claims with the sufficient specificity required by M.P.E.P. 2131.03. Thus, Mardiguan does not anticipate the claims. Applicants request that the rejection be withdrawn.

Claim 56 is Not Anticipated by Mardiguan

The Office also rejects claim 56 under 35 U.S.C. § 102(e) as allegedly anticipated by Mardiguan. While claim 56 is a product-by-process claim, the Office states that determination of the patentability of the claimed product is based on the product itself, and contends that the limitations of the claimed product are met by

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Mardigulan. (Office Action at pages 4-5.) Applicants respectfully disagree and traverse the rejection.

Applicants maintain that it is well established in the field of heparin research, prior to the filing date of the subject application, that "commercial LMW heparins are not chemically equivalent. The differences are primarily the result of the chemical or enzymatic process used in their depolymerization. The chemical inequivalence of these preparation results in different molecular weights, degrees of sulfation and oligosaccharides maps. These altered physical-chemical properties affect anticoagulant activities of LMW heparins making them bioinequivalent." Linhardt *et al.* (1990) J. Med. Chem. 1639-1645, 1643 (copy enclosed).

As noted by the Office, methods of preparing at least one salt chosen from alkali and alkaline-earth metal salts of at least one sulphated polysaccharide of heparin wherein a phosphazene, imidazolate, or 1,5,7 triazabicyclo-[4.4.0]-dec-5-ene is used as a base in the depolymerization step are neither taught or suggested by the prior art. Given that the physical-chemical properties of LMW heparins are the result of the process by which they are made and that the process claimed herein is novel and non-obvious, Applicants respectfully maintain that claim 56, which is drawn to a product of such novel and non-obvious process, is also novel and non-obvious. See M.P.E.P. 2113 ("The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially . . . where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product."), citing *In re Gamero*, 412 F.2d 276, 279.

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162 U.S.P.Q. 221, 223 (CCPA 1979). Applicants request that the rejection be withdrawn.

Claims 38-46 Are Not Anticipated by Mardiguian

The Office also rejects 38-46, under 35 U.S.C. § 102(e), as allegedly anticipated by Mardiguian. The Office contends that claims 38-46, which recite methods of treating venous and/or arterial thrombosis and depend from claims 1, 2 or 57, are anticipated by Mardiguian's alleged disclosures of compositions that anticipate claims 1, 2, or 57, and that those compositions are useful for the treatment of venous and arterial thrombosis. (Office Action at page 5.)

As claims 1, 2, and 57 are not anticipated by Mardiguian, Applicants respectfully maintain that the methods of treating venous and/or arterial thrombosis using a composition of claim 1, 2, or 57 likewise are not anticipated by Mardiguian. See M.P.E.P. 2116.01. Applicants request that the rejection be withdrawn.

Information Disclosure Statement

Applicants submit herewith an Information Disclosure Statement and PTO 1449 form, listing three references cited in the foreign prosecution of the corresponding Taiwanese patent application. This Information Disclosure Statement is being filed before the mailing date of a first Office Action following an RCE.

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Conclusion

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated by nor obvious in view of the cited prior art. Applicants respectfully request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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